A Multicomponent Synthesis of Stereodefined Olefins via Nickel Catalysis and Single Electron/Triplet Energy Transfer

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Unsaturated carbon–carbon bonds are one of the most common and important structural motifs in many organic molecules, stimulating the continuous development of general, efficient, and practical strategies for their functionalisation. Herein, we report a one-pot difunctionalisation of alkynes via a photoredox/nickel dual catalysed three-component cross coupling reaction under mild conditions, providing access to a series of highly important trisubstituted alkenes. Notably, in contrast to the traditional methods which are based on the steric hindrance of the substrates to control the reaction selectivity, both *E*- and *Z*- isomers of trisubstituted alkenes which are often energetically close, can be obtained via choosing an appropriate photocatalyst with a suitable triplet state energy. Beyond the immediate practicality of this transformation, this newly developed methodology might inspire the development of diverse and important one-pot functionalisations of carbon-carbon multiple bonds via photoredox and transition-metal dual catalysed multi-component reactions.

Multi-component reactions are a class of useful transformations employed widely for the efficient synthesis of diverse compounds in organic synthesis^{1–6}. In the past decades, significant progress has been achieved in the field of difunctionalisation of carbon-carbon multiple bonds via multi-component reactions. However, the employed methods rely largely on the use of organometallic species such as Grignard reagents⁷, organoboron⁸ and organolithium⁹ reagents and require high temperatures or multistep reactions. More recently, radical-mediated transformations have been developed, providing a good alternative for the one-pot difunctionalisation of these motifs. In this case, a radical is generally generated from a suitable precursor via a single electron transfer process by using O₂¹⁰, transition metal species^{11–14} or photocatalysts^{15–17}. The generated radical adds to the alkyne or alkene moiety to give a vinyl or alkyl radical intermediate. For transition metal catalysed transformations, various radical precursor including sulfonyl chlorides¹¹, activated alkyl bromides¹², and fluoroalkyl iodides¹³ were used in the cross-coupling reactions with organoboron reagents. For photoredox catalysed protocols, in most of the cases, the generated vinyl or alkyl radical intermediate undergoes subsequently hydrogen atom transfer (HAT), CO₂ fixation¹⁶ or another SET process to give a carbocation which can be attacked by a nucleophile¹⁷ under mild conditions. We questioned whether it would be possible to exploit the vinyl or alkyl radical intermediate, generated via a photoredox catalytic pathway, in transition-metal catalysed cross couplings, thus developing a photoredox and transition-metal dual catalysed multi-component cross coupling platform under mild conditions, transformation which has not been accomplished before. Moreover, the *E/Z* isomerisation induced by the energy transfer of the generated trisubstituted alkene bearing two similar aryl groups on the same carbon atom may be controlled via a carefully tuned photocatalyst with a suitable triplet energy (Fig. 1b), which is highly challenging if compared to a planar, conjugated *E* isomer and twisted, deconjugated *Z* isomer (Fig. 1a)¹⁸. Recently excellent two-component cross coupling reactions have been achieved in the field of C-C and C-heteroatom bond formation via photoredox and nickel dual catalysis^{19–26}.

Inspired by these results, we envisaged that a three-component cross coupling reaction involving aryl halides, sodium sulfinates and alkynes is feasible via this strategy, enabling the difunctionalisation of alkynes in a one-pot manner, under mild conditions. However, there are several challenges to be addressed, which mainly include α -substituted vinyl sulfones generation via Markovnikov addition of the sulfonyl radical to terminal alkynes²³, aromatic sulfone formation via cross coupling of sulfinate salts with aryl halides²⁴ and control of the *Z/E* ratio of the generated trisubstituted alkenes. Here we report the aryl-sulfonylation of alkynes with high chemo-, regio-, and stereoselectivity (Fig. 1c). The utility and applicability of this methodology was demonstrated by the high tolerance toward numerous functional groups, the functionalisation of complex molecules which is relevant for the late stages of multistep syntheses, the success of gram-scale reactions, and the transformation of the generated products into further valuable organic

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compounds. Our results indicate the reaction outcome is depending on the photocatalyst, that is involved in single electron transfer processes or both, single electron transfer and energy transfer processes.

Figure 1 | Multicomponent cross-coupling reaction under mild conditions and its main challenges. **a**, Conventional energy transfer induced isomerisation between planar, conjugated *E* isomer and twisted, deconjugated *Z* isomer. **b**, Challenging *E/Z* isomerisation between two twisted and deconjugated isomers. **c**, Our proposed multicomponent cross-coupling protocol and its main challenges.

Results

Mechanistic design. A proposed mechanism for our designed three-component cross coupling platform is shown in Fig. 2. Initially, in the photocatalytic cycle, the Ir^{III} or Ru^{II} complex absorbs visible light and promotes a long-lived ^{*}Ir^{III} or ^{*}Ru^{II} triplet excited state, which then oxidises the radical precursor to the corresponding radical along with formation of the Ir^{II} or Ru^I reductant. The resulting radical enters the nickel catalytic cycle by adding to a Ni^I complex, which subsequently undergoes reduction, 1,2 migratory insertion of alkyne, Ni-assisted *anti/syn* isomerisation, oxidative addition of the aryl halide and reductive elimination to give the three-component *anti*-addition product **P_{anti}**. Noteworthy, depending on the photocatalyst, an energy transfer (ET) process promoting the isomerisation of the product can be involved in the transformation.^{18,27-29} The use of photocatalysts with a triplet state energy below that of the excited state of the *anti*-addition product **P_{anti}**, which is $E_T(\text{PC}) < E_T(\text{P}_{\text{anti}})$, results in little or no isomerisation, giving the *anti*-addition product **P_{anti}** as single product. In contrast, the use of photocatalysts with a triplet state energy higher than that of both isomers, which is $E_T(\text{PC}) > E_T(\text{P}_{\text{syn}}) > E_T(\text{P}_{\text{anti}})$, affords the products with low *Z/E* ratios. However, the use of photocatalysts with a triplet state energy higher than that of the excited state of the *anti*-addition product **P_{anti}** but lower than that of the corresponding isomeric product **P_{syn}** which is $E_T(\text{P}_{\text{syn}}) > E_T(\text{PC}) > E_T(\text{P}_{\text{anti}})$, leads to effective isomerisation, delivering mainly the corresponding isomeric product **P_{syn}** (Fig. 2a).

Figure 2 | Mechanistic design of the newly developed three-component reaction. **a**, Excitation of the photocatalyst by visible light to produce a long-lived triplet excited state which oxidises the radical precursor to the corresponding radical (**photocatalytic cycle**) which enters the nickel catalytic cycle. The resulting Ni-complex undergoes reduction, 1,2-migratory insertion of alkyne, Ni-assisted isomerisation, oxidative addition of aryl bromide and reductive elimination to give the anti-addition three-component product **P_{anti}** (**nickel catalytic cycle**). In addition, isomerisation can be achieved by triplet energy transfer with the photocatalyst to give the isomeric product **P_{syn}** (**triplet–triplet energy transfer**). **b**, Triplet state energy of photocatalysts measured in DMF.

Reaction development. With this design in mind, we started our study by evaluating the cross-coupling reaction between 4-bromobenzonitrile, phenylacetylene and sodium 4-methylbenzenesulfonate in the presence of photocatalyst **2**, NiCl₂·dme and dtbbpy ligand (**L1**) for 12 h. However, only unwanted two-component reaction products such as the corresponding sulfonlated arene (21%)²⁴ and α -substituted vinyl sulfone (6%)²³ as well as 4-hydroxybenzonitrile (20%) were obtained. Given the essential role of ligands in cross-coupling transformations, we next evaluated several nitrogen and phosphine-containing ligands (see Supplementary Table 1). Notably, 95% yield of the desired three-component cross coupling product **5** (*Z/E* ratio 89:11) was obtained when ligand **4** was used. Moreover, further investigation of a series of photocatalysts showed that a reverse *Z/E* ratio could be achieved upon using photocatalysts possessing different triplet state energies (Supplementary Table 4). When photocatalyst **1** was used, we obtained the desired product **5** in 49% yield with 62:38 *Z/E* ratio. However, when Ru-based photocatalyst **3** was used, the *Z/E* ratio reached the level of 1:99, emphasizing the unique feature of the developed photoredox and nickel catalysed three-component cross coupling transformation (Fig. 2b). Control experiments demonstrated that no desired product was generated in the absence of light, photocatalyst, nickel catalyst or ligand (Supplementary Table 6).

Scope of the reaction. With the optimised reaction conditions in hand, we first examined the scope of the reaction with respect to the aryl halides using the Ru-based photocatalyst **3**. As shown in Fig. 3a, a series of aryl bromides and aryl iodides bearing

electron-withdrawing, electron-neutral and electron-donating substituents underwent this transformation providing the corresponding products **5-22** in moderate to excellent yields. 2-Methoxyiodobenzene gave a lower yield compared to 4-methoxyiodobenzene, indicating that the reaction was slightly hampered by increasing the steric hindrance (**20** and **21**). Notably, substrates bearing common sensitive functional groups such as aldehyde, unprotected aniline and phenol underwent the reaction and gave the corresponding products **11**, **23** and **24** in moderate to high yields, which are hard to achieve using traditional synthetic methods. In addition, this transformation proceeded chemoselectively with aryl iodide over fluoride, chloride and bromide, enabling further functionalisation of the generated products (**25-27**, 83-99%). Moreover, disubstituted aryl halides and bicyclic substrates including dioxole, phthalide, phthalimide, and naphthyl derived halides could also be applied in reaction with good to high efficiency (**28-34**, 61-90%). It is noteworthy that this mild three-component cross coupling method could be readily extended to pharmaceutically relevant heteroaromatic halides. Not only electron-deficient but also electron-rich nitrogen containing heterocyclic halides including quinoline, pyridines, pyrimidine, and pyrazole derivatives could undergo this reaction in good to excellent yields (**35-41**, 64-95%). The reaction proceeded smoothly also with thiophene-derived halides, providing the corresponding products **42** and **43** in good to high yields. Encouraged by these results, we continued to explore the substrate scope with respect to the structure of alkynes under the standard reaction conditions (Fig. 3b). The generality of alkynes scope was well illustrated by the tolerance of a series of functional groups such as ester, fluoride, chloride, bromide, alkyl, methoxy, methylthio, amine, acetal and boronic ester groups (**44-60**). Notably, the steric properties of the alkynes have no obvious effects on the reaction efficiency (**49-51** and **54-55**). Also, 3-ethynylthiophene gave the desired product in good yield (**61**). More importantly, the scope is not limited to aromatic terminal alkynes, cyclohexenyl alkyne and internal alkynes were also suitable substrates for this catalytic system (**62-64**). However, the size of the alkyne substituent has a significant effect on the transformation efficiency and the yield decreased as the size of the group increased.

Figure 3 | Substrate scope of aryl halides and alkynes for the photoredox/nickel dual catalysed aryl-sulfonylation of alkynes using Ru photocatalyst **3.**

Reaction conditions: Aryl halide (0.4 mmol), alkyne (0.4 mmol), sodium 4-methylbenzenesulfinate (0.2 mmol), Ru photocatalyst **3** (0.002 mmol), NiCl₂·dme (0.02 mmol), ligand **4** (0.02 mmol), degassed DMF (2 mL), room temperature, irradiation with 7.4 W blue LED strips with fan cooling for 24 h. Yield after purification. *From aryl bromide †From aryl iodide ‡ The Z/E ratio of product **24** is 37:63. § The Z/E ratio of product **33** is 10:90. # Alkyne as limiting reagent (0.2 mmol), aryl halide (0.4 mmol), sodium sulfinate (0.4 mmol).

Next, we investigated the scope of sodium sulfinates (Fig. 4a). A series of structurally diverse sodium aryl sulfinates bearing electron-donating as well as electron-withdrawing functional groups underwent the reaction smoothly (**65-72**). While a substrate possessing a methyl group in the ortho position of the aromatic ring worked well (**67**, 90%), a more sterically hindered substrate gave the desired product in moderate yield (**68**, 53%). Moreover, sodium naphthyl and thienyl sulfinates were also suitable substrates (**73**, 98%, **74**, 97%). Remarkably, sodium alkyl sulfinates also showed high reactivity in this catalytic system. Sodium

sulfonates bearing methyl, ethyl, cyclohexyl, and cyclopropyl groups gave the corresponding products **75-78** in 78-92% yield. Finally, a series of complex molecules were evaluated in this protocol (Fig. 4b). For example, aryl halides bearing galactopyranose, probenecid, pregnenolone, cholestanol, and adamantanecarboxylic acid motifs reacted with phenylacetylene and sodium 4-methylbenzenesulfinate to give the appropriate products **79-83** in moderate to high yields. Estrone and δ -tocopherol derived alkynes underwent reaction with 4-bromobenzonitrile and sodium 4-methylbenzene-sulfinate to give the corresponding products **84** and **85** with good efficiency. Notably, trisubstituted alkene **86**, bearing two complex motifs, was achieved in 84% yield via this strategy.

Figure 4 | Substrate scope of sodium sulfonates and complex molecules for the photoredox/nickel dual catalysed aryl-sulfonylation of alkynes using Ru photocatalyst 3. Reaction conditions: Aryl halide (0.4 mmol), alkyne (0.4 mmol), sodium sulfinate (0.2 mmol), Ru photocatalyst **3** (0.002 mmol), $\text{NiCl}_2\cdot\text{dme}$ (0.02 mmol), ligand **4** (0.02 mmol), degassed DMF (2 mL), room temperature, irradiation with 7.4 W blue LED strips with fan cooling for 24 h. Yield after purification. The reactions of complex molecules **81, 82, 84-86** were conducted on 0.1 mmol. *From aryl bromide †From aryl iodide ‡Aryl halide as limiting reagent (0.2 mmol), alkyne (0.4 mmol), sodium sulfinate (0.4 mmol). §The *Z/E* ratio of product **80** is 22:78.

Next, the substrate scope was evaluated with respect to the three components in the presence of Ir-based photocatalyst **2** which, in contrast to Ru-based photocatalyst **3**, promotes a reaction pathway involving SET, nickel catalysis, and energy transfer (Fig. 5). Aryl halides bearing electron-withdrawing groups and heterocyclic aryl halides gave mainly the corresponding isomerised products

87-96 in high yield with efficient stereoselectivity. In contrast, aryl halides possessing electron-donating groups such as methyl, *tert*-butyl, and methoxy failed to undergo isomerisation, giving the corresponding *anti*-addition products **18-20**. Alkynes bearing both electron-donating and electron-withdrawing groups on the aromatic rings and 3-ethynylthiophene led to efficient isomerisation of the desired products (**97-101**). Similarly, sodium aryl sulfonates bearing methoxy and fluoride groups and sodium alkyl sulfonates also gave the corresponding products **103-109** in good yields with good isomeric ratios. Notably, the isomerisation occurred with reasonable stereoselectivity when complex molecules were exploited (**108-111**), even when two complex precursors were used in the reaction (**109**).

Figure 5 | Substrate Scope for the photoredox/nickel dual catalysed aryl-sulfonylation of alkynes using Ir photocatalyst 2. Reaction conditions: Aryl bromides (0.4 mmol), alkynes (0.4 mmol), sodium sulfonates (0.2 mmol), Ir photocatalyst **2** (0.002 mmol), NiCl₂·dme (0.02 mmol), ligand **4** (0.02 mmol), degassed DMF (2 mL), room temperature, irradiation with 34 W blue LED with fan cooling for 24 h. Yield after purification. The values in parenthesis represent the ratio of the two isomers (*P*_{syn} : *P*_{anti}) which was determined by ¹H NMR analysis. The reaction of complex molecules **108-110** were conducted on a 0.1 mmol scale.

Applications of this protocol. Importantly, gram-scale reactions were successfully conducted using the standard substrate 4-bromobenzonitrile, giving both *E* and *Z* products in 92% and 96% yield, respectively. Although the catalytic process using Ir **2** gave the product with 91:9 *Z/E* stereoselectivity, the pure *Z* isomer could be obtained in good yield after one simple recrystallisation of the product. Moreover, further functionalisation of the generated pure *E* and *Z* products were conducted via the cross-coupling reaction with the activated primary amine (pyridinium salt) under irradiation with blue LEDs in the absence of photocatalyst³⁰,

affording the corresponding products **112** and **113** in good yield with good stereoselectivity. Also, the reaction of product **114** with 1-phenylpyrrolidine and *N*-Boc proline allowed alkylation of the alkene (**115** and **116**) (Fig. 6a)³¹. Notably, this newly developed multicomponent methodology could also be easily extended to other radical precursor such as feedstock carboxylic acid. With minor reaction condition modifications, both cyclic and acyclic *N*-Boc-protected amino acid could give the desired three-component products **117-119** in good yields with good stereoselectivity (Fig. 6b). These applications demonstrate the great potential synthetic value of this visible light mediated protocol.

Figure 6 | Gram-scale reactions and Applications. **a**, Gram-scale reactions and further transformations of the generated products. **b**, The utilisation of another type of radical precursor.

Mechanistic study. To gain some insight into the mechanism, we conducted a series of control experiments. Stern-Volmer quenching experiments of all three starting materials show that only sodium 4-methylbenzenesulfinate quenches the photocatalyst **2**, suggesting that the process involves sulfonyl radical intermediates (Fig. 7a). Monitoring the reaction progress and representing the yield and *Z/E* ratio vs reaction time shows that *E* isomer **5** was obtained prior to *Z* isomer **87** which indicates the SET process is faster than ET process (Fig. 7b). The emission spectra of the three photocatalysts were measured, and, as shown in Fig. 7c, λ_{max} (**Ir 1**) = 481.6 nm, λ_{max} (**Ir 2**) = 563.7 nm, λ_{max} (**Ru 3**) = 609.3 nm, which means that the triplet state energy has the following trend: **Ir 1** > **Ir 2** > **Ru 3** (E_{T} of 59.4, 50.7 and 46.9 kcal/mol, respectively). In addition, we observed efficient isomerisation for pure *E*-**5** product in the presence of **Ir 2**, almost no isomerisation for pure *Z*-**87** product in the presence of **Ru 3**, and inefficient isomerisation for pure *Z*-**87** product in the presence of **Ir 1**, indicating the role of triplet-triplet energy transfer for the isomerisation (Fig. 7d).

Figure 7 | Mechanistic investigations. **a**, Stern-Volmer quenching experiments of the starting materials. **b**, Reaction progress monitoring the yield and *Z/E* ratio vs reaction time. **c**, Emission spectra measurement of photocatalysts. **d**, *Z/E* isomerisation via energy transfer using photocatalysts possessing different triplet state energies.

To further support the proposed mechanism, we examined the nickel catalytic cycle in detail, using DFT based calculations. The energy profile is displayed in Fig. 8a and the structures of the transition states are shown in Fig. 8b. It is well known that dual photoredox/Ni-catalysed processes are terminated by the reductive elimination from Ni^{III} with the formation of common intermediate $\text{Ni}^{\text{I}}\text{-Br}$ ³². Therefore, $\text{Ni}^{\text{I}}\text{-Br}$ **E** was assumed as starting complex for the investigation of the nickel catalytic cycle. The catalytic process is initiated by the barrierless addition of the sulfonyl radical to Ni^{I} , leading to intermediate **F** with a free energy gain of 22.0 kcal/mol (Fig. 8)^{33, 34}. As alternatives, we explored the reduction of Ni^{I} to Ni^0 via SET by Ir^{II} **2** (Supplementary Fig. 13), and the addition of the sulfonyl radical to the alkyne with formation of a vinyl radical (Supplementary Fig. 14), but we found that these routes are clearly disfavoured. Next, irreversible SET from Ir^{II} **2** to **F** leads to the formation of the Ni^{I} intermediate **G**, a step exergonic by 17.9 kcal/mol. The next section in the cycle is coordination and migratory insertion of the alkyne. It starts with the almost thermoneutral coordination of the alkyne to **G**, leading to **H**, followed by rearrangement of the sulfinate from a Ni-S to a Ni-O bonding mode, leading to the similarly stable intermediate **I** with a relatively low energy barrier of only 7.8 kcal/mol. The sulfonyl group of **I** is in a suitable orientation to promote nucleophilic attack to the C^{α} atom of the alkyne through the sulfur atom. This step occurs via the five membered cyclic transition state **I-J** and it has an activation barrier of 19.3 kcal/mol. The resulting vinyl intermediate **J**, presenting an *anti* orientation of the sulfonyl and phenyl substituents, is 4.3 kcal/mol lower in energy than **I**. Migratory insertion of the sulfonyl group to the C^{β} atom of the alkyne was found to be disfavoured by 2.5 kcal/mol (Supplementary Fig. 18).

At this stage, intermediate **J** can either undergo direct oxidative addition of the aryl-bromide via transition state **J-L'**, with an activation energy of 26.6 kcal/mol, leading to the final product **P_{syn}** (red pathway in Fig. 8a), or it can undergo a two step route (blue pathway in Fig. 8a), starting with the *anti* to *syn* isomerisation of the vinyl group, **J** to **K**, followed by oxidative addition of the aryl-bromide, **K** to **L**, leading to the final product **P_{anti}**. The *anti* to *syn* isomerisation occurs via transition state **J-K**, with an energy barrier of 23.3 kcal/mol, and it involves a rotation around the C-C bond. The relatively low energy barrier for this rotation is due to

delocalisation of the π -system of the vinyl bond to include the Ni atom in transition state **J-K**, which reduces the double bond character of the C=C (see Supplementary Table 7). The oxidative addition of the aryl-bromide occurs via transition state **K-L**, laying 1.9 kcal/mol below transition state **J-K**. Comparison of the blue and red routes in Fig. 8a indicates that the two step route is favoured, as transition state **J-K** is favoured by 3.3 kcal/mol over transition state **J-L'**, which implies that intermediate **J** preferentially evolves to intermediate **L**. This result is consistent with the experimental selective formation of **P_{anti}** (Fig. 7d).

Release of the product via reductive elimination from **L** requires isomerisation of the system to the more stable intermediate **N**, which presents a *cis* disposition of the aryl and vinyl groups. The lowest pathway we found involves Br⁻ dissociation/coordination via intermediate **M**. The reductive elimination of product **P_{anti}** from **N** occurs via transition state **N-E** and a low energy barrier of only 5.0 kcal/mol.

Figure 8 | Computational investigation of the nickel catalytic cycle. a, Proposed mechanism of nickel catalytic cycle based on DFT calculations. **b,** DFT optimised geometries of all transition states involved in the lowest energy pathway. Bond lengths are in Å.

Conclusion

In conclusion, we have developed a three-component cross coupling reaction involving aryl halides, sodium sulfinates and alkynes. The protocol exhibits high tolerance towards various functional groups and could be readily extended to diverse complex molecules. The proposed mechanism features the combination of single electron transfer (SET) with nickel catalysis and single electron transfer (SET), nickel catalysis followed by energy transfer (ET), enabling the generation of trisubstituted alkene isomers. We anticipate that this protocol will provide a platform for other mild multi-component cross coupling reactions in organic synthesis.

Methods

General procedure for the catalytic reactions using Ru 3 as photocatalyst. A dry reaction tube equipped with a Teflon-coated magnetic stir bar was charged with aryl

halide (0.4 mmol, 2 equiv., if solid), sodium sulfinate (0.2 mmol, 1 equiv.), Ru **3** (2.2 mg, 0.002 mmol, 1 mol%), NiCl₂-dme (4.4 mg, 0.02 mmol, 10 mol%), 4,4',4''-tri-*tert*-butyl-2,2':6',2''-terpyridine (8.0 mg, 0.02 mmol, 10 mol%) and alkyne (0.4 mmol, 2 equiv., if solid). It was capped with a rubber septum, evacuated and backfilled with argon (3 times). Then, degassed DMF (2.0 mL), aryl halide (0.4 mmol, 2 equiv., if liquid) and alkyne (0.4 mmol, 2 equiv., if liquid) were added via syringe. The reaction mixture was stirred at room temperature for 24 h under irradiation with 7.4 W blue LED strips with fan cooling. Upon completion, the solution was diluted with H₂O (10 mL) and EtOAc (10 mL). The layers were separated, then the aqueous layer was extracted with EtOAc. The combined organic layer was washed with H₂O (20 mL) and brine (20 mL). The organic layer was dried with anhydrous Na₂SO₄, then concentrated under vacuum and purified by column chromatography on silica gel using hexane: EtOAc as eluent to get the corresponding pure product (The reaction of complex molecules **81**, **82**, **84-86** were conducted on 0.1 mmol with 2 mL DMF solvent).

General procedure for the catalytic reactions using Ir **2 as photocatalyst.** A dry reaction tube equipped with a Teflon-coated magnetic stir bar was charged with aryl halide (0.4 mmol, 2 equiv., if solid), sodium sulfinate (0.2 mmol, 1 equiv.), Ir **2** (2.1 mg, 0.002 mmol, 1 mol%), NiCl₂-dme (4.4 mg, 0.02 mmol, 10 mol%), 4,4',4''-tri-*tert*-butyl-2,2':6',2''-terpyridine (8.0 mg, 0.02 mmol, 10 mol%) and alkyne (0.4 mmol, 2 equiv., if solid). It was capped with a rubber septum, evacuated and backfilled with argon (3 times). Then, degassed DMF (2.0 mL), aryl halide (0.4 mmol, 2 equiv., if liquid) and alkyne (0.4 mmol, 2 equiv., if liquid) were added via syringe. The reaction mixture was stirred at room temperature for 24 h under irradiation with 34 W Kessil blue LED lamp with fan cooling. Upon completion, the solution was diluted with H₂O (10 mL) and EtOAc (10 mL). The layers were separated, then the aqueous layer was extracted with EtOAc. The combined organic layer was washed with H₂O (20 mL) and brine (20 mL). The organic layer was dried with anhydrous Na₂SO₄, then concentrated under vacuum and purified by column chromatography on silica gel using hexane: EtOAc as eluent to get the corresponding pure product (The reaction of complex molecules **108-110** were conducted on 0.1 mmol with 2 mL DMF solvent).

Computational details. All DFT-calculations were performed using Gaussian 09, Revision D.01³⁵. The geometry optimisation and frequency analysis were performed using the PBE functional^{36,37}. The split-valence plus one polarisation function def2-SVP basis set was used for non-metal atoms and the triple- ζ basis set def2-TZVP was used for metals^{38,39}. In all cases, the default integral grid (Fine Grid) was employed. Frequency calculations were performed in order to obtain thermal corrections (298 K) and to confirm the nature of the stationary points (minima with no imaginary frequency or transition states with one imaginary frequency). For transition state structures, IRC calculations were undertaken to confirm that the transition states were connected to the correct minima. For better energetics, single point energy calculations were performed using the hybrid-meta-GGA M06 functional⁴⁰ with the def2-TZVPP basis set^{38,39} for all atoms. Restricted DFT was employed for species in the singlet spin state, while unrestricted DFT was used for species in the doublet or triplet spin states. The implicit SMD solvent model⁴¹ was used to account for solvent effects, *N,N*-Dimethylformamide (DMF, $\epsilon = 37.2$). Unless specified otherwise, Gibbs free energy, *G*, was used throughout the text. The *G* value was obtained by augmenting the in solvent electronic energy *E*_{el} at the M06(SMD-DMF)/(def2TZVPP) level with the respective free energy corrections at the PBE/def2-SVP(C,H,N,O,S,Br)/def2-TZVP(Ni,Ir) level in gas phase. As it is known that translational and rotational entropies in solution for association/dissociation processes are overestimated/underestimated, and that the deviation in the free energies is approximately 1.89 kcal/mol from the standard state (1 atm) to 1 M in solution^{42,43}, we have reduced by 1.89 kcal/mol the free energy for addition steps and we have added 1.89 kcal/mol to the free energy of the dissociation steps. Natural bond orbital (NBO) analysis were performed using the *NBO 3.1* program^{44,45}. The geometries were realised using CYLview, 1.0b⁴⁶. The Mayer bond order was calculated using the Multiwfn 3.5 software⁴⁷.

Data availability

The X-ray crystallographic coordinates for structures of **5** and **87** reported in this Article have been deposited at the Cambridge Crystallographic Data Centre (CCDC) under deposition numbers CCDC 1914140 (**5**) and 1914141 (**87**). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Experimental procedures and characterisation of the new compounds are available in the Supplementary Information. All other data are available from the authors upon reasonable request.

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Author contributions

C.Z., H.Y. and M.R. conceived and designed the experiments. C.Z., H.Y. performed and analyzed the experiments. I.A. conducted X-ray crystal structure analysis. C.Z., B.M. and L.C. performed the theoretical calculations. All authors discussed the results and contributed to the manuscript.

Competing interests

The authors declare no competing interests.